REMARKS

Claims 62-108 were pending in the subject application. By this Amendment applicants have canceled claims 62-108 and added new claims 109-146. Accordingly, claims 109-146 are pending and under examination.

Election/Restriction

Applicants have noted the restriction requirement previously imposed by the Examiner including the application of the restriction requirement to previously pending claims 62-108. Applicants' new claims 109-146 have been drafted in compliance with the imposed restriction requirement. However, for the record, applicants maintain that the application of the restriction requirement to previously pending claims 62-108 in so far as it resulted in the withdrawal of certain claims from consideration was improper for reasons of record.

Rejections under 35 U.S.C. §112, first paragraph

On page 3 of the November 10, 2003 Office Action the Examiner rejected claims 62-65, 67-77, 79-85 and 101-108 under 35 U.S.C. 112, first paragraph, alleging that, while the specification provides enablement for a method of decreasing expression of a delta-12 fatty acid desaturase by transforming a cotton plant with a construct comprising either a full length delta-12 fatty acid desaturase gene in antisense or with a construct comprising inverted repeats of a delta-12 fatty acid desaturase gene that are 850 bp and optionally with a 92 bp intervening sequence, as well as the transgenic cotton plants and seeds produced by said method, does not reasonably provide enablement for the same method wherein the construct merely comprises a 20 nucleotide fragment of a delta-12 desaturase gene.

The Examiner alleged that the specification only discloses a method of decreasing expression of a delta-12 fatty acid desaturase by transforming a cotton plant with a construct comprising either a full length delta-12 fatty acid desaturase gene in antisense or with a construct comprising inverted repeats of a delta-12 fatty acid desaturase gene that are 850 bp and optionally with a 92 bp intervening sequence, as well as the transgenic cotton plants and seeds produced by said method, referring to page 92. The Examiner alleged that the specification does not teach use of constructs having as little as 20 nucleotides for decreasing expression of the delta-12 desaturase gene, in either sense or antisense orientation, or as inverted repeats. The Examiner alleged that Stam et al. (submitted by applicants with the response filed January 21, 2003) teach that the mechanism of antisense transgenes to degrade complementary RNAs is poorly understood, and that small antisense molecules have difficulty accessing complementary RNAs, referring to page 27 of Stam et al.

In response, without conceding the correctness of the Examiner's position, but merely to advance the prosecution of the subject application, applicants have rewritten the claims to recite a process where the gene construct encodes a ribonucleotide molecule which reduces expression of the endogenous cotton *gh*FAD2-1 gene. The new claims do not require using a 20 nucleotide fragment in the process. Applicants contend that the rejection of record does not apply to the new claims.

Specifically, applicants have in their specification described and successfully *exemplified* several gene constructs encoding a ribonucleotide molecule which reduces expression of the endogenous cotton *gh*FAD2-1 gene. As of the date of applicants' invention, one skilled in the art upon studying applicants'

specification and exemplified gene constructs would readily be able to make and use other gene constructs that encode a ribonucleotide molecule which reduces expression of the endogenous cotton *gh*FAD2-1 gene. Nothing of record suggest otherwise.

Accordingly, the rejection under 35 U.S.C. § 112, first paragraph, is moot as to canceled claims 62-108, and does not apply to the new claims 109-146.

35 U.S.C. § 103 (a) - U.S. Patent 6,372,965 (Lightner et al.)

In Section 6 of the November 10, 2003 Office Action, the Examiner rejected claims 62, 63, 67-75, 79-85, 101, 102 and 106-108 under 35 U.S.C. §103 as allegedly unpatentable over U.S. Patent No. 6,372,965 to Lightner et al.

The Examiner alleged that Lightner et al. teach transformation of plants with at least portions of a delta-12 desaturase gene in sense or antisense orientation and operably linked to a seed specific promoter to modify the endogenous oil content of a plant, referring to columns 27-28. The Examiner also alleged that Lightner et al. teach a nucleotide sequence (SEQ ID NO: 11, nucleotides 1175-1203) which has more than 20 nucleotides that are identical to SEQ ID NO:3 at nucleotide 1057-1085, and the desirability of transforming cotton, referring to column 30.

The Examiner acknowledged that Lightner et al. does not specifically teach using the soybean lectin promoter or exemplify a transformed cotton plant. However, the Examiner alleged that given the recognition of those of ordinary skill in the art of the value of transforming a plant with at least portions of a delta-12 desaturase gene in sense or antisense orientation and operably linked to a seed specific promoter to modify the

endogenous oil content of a plant, as taught by Lightner et al., and given the alleged teaching of Lightner et al. of the desirability of transforming a cotton plant to modify the endogenous oil in the seed, it would have been obvious to use the teachings of Lightner et al. to transform a cotton plant to produce a cotton plant with modified endogenous oil content, and it would have been obvious to substitute other seed preferred promoters to have the same effect. The Examiner then alleged that the claimed invention would have been *prima facie* obvious as a whole at the time it was made, especially in the absence of evidence to the contrary.

In response, without conceding the correctness of the Examiner's position, but merely to advance prosecution of the subject application, applicants have rewritten the claims to recite a process for producing a cotton plant wherein the fatty acid of the seed oil of the plant comprises 58.5% oleic acid, the corresponding cotton plant, seed and seed oil. Lightner et al. do not teach or suggest such a method.

As noted in the subject specification on page 6, line 26 to page 7, line 5, there was "no reported modification (prior to applicants' invention) of fatty acid metabolism in cotton, using traditional plant breeding, mutational breeding, or recombinant DNA approaches." Stated otherwise, there was no knowledge, supported by experimental testing, in the prior art of which enzymatic step was rate limiting in fatty acid biosynthesis in cotton. Accordingly, the effect of down-regulating delta-12 desaturase in cotton was unknown prior to applicants' invention. More importantly, the extent of the effect of down-regulating the delta-12 desaturase in cotton was unknown.

As the Examiner is aware, and as the specification describes on

page 7, "[t]he tetraploid nature of cotton, and the existence of large families of specific fatty acid biosynthesis genes makes it difficult to determine those genes which, by virtue of being expressed in a seed-specific manner are suitable targets for silencing with a view to modifying oil seed composition." One of skill in the art would have known that cotton, being tetraploid, has two copies of every gene. Moreover, the presence of multiple members of delta-12 desaturase genes in cotton (at least three members per genome x two copies = at least six genes) would have made the selection of a gene to target unpredictable prior to applicants' invention.

Furthermore, the applicants' new process claims recite reducing expression of the ghFAD2-1 gene, not any delta-12 desaturase gene. This selection was also unpredictable. Applicants found that ghFAD2-1 and ghFAD2-2 genes from cotton have homology (around 60-70% identity) with the delta-12 desaturase family of mixed function mono-oxygenase enzymes in plants. Different members of this family within this range of identities are known to catalyse a range of reactions at the delta-12 position of C18 fatty acids including but not limited to desaturation (conversion of carbon single bond to double bond), acetylenation (conversion of carbon double bond to triple bond), epoxygenation (conversion of carbon double bond to epoxy bridge group), conjugation (migration of carbon double bond to adjacent position) and hydroxylation (addition of hydroxy group). Identification of a sequence as belonging to this family of enzymes based on significant sequence similarity to known members of the family in other plant species is not at all predictive of the functionality of the enzyme, particularly in species such as cotton which synthesizes unusual fatty acids, such as cyclopropanoic fatty acids (CPFAs), in addition to the usual fatty acids. Thus, demonstration that a gene from cotton is a

member of the delta-12 desaturase/acetylenation/epoxygenation etc. family does not predict that inhibition of the gene would increase oleic acid content of the cotton seed oil.

Yet furthermore, and most importantly, the prior art provided no expectation that the extent of the effect of reducing the expression of the ghFAD2-1 gene in cotton would be the production of a cotton plant wherein the fatty acid of the seed oil of the plant comprises 58.5% oleic acid.

In conclusion, as explained above, production of a cotton plant wherein the fatty acid of the seed of the plant comprises 58.5% oleic acid, the corresponding cotton plant, seed and seed oil, was not obvious from the prior art. Accordingly, the rejection under 35 U.S.C. § 103 over Lightner et al. does not apply to applicants' new claims.

35 U.S.C. § 103 (a) - U.S. Patent 6,372,965 (Lightner et al.) and U.S. Patent 5,952,546 (Bedbrook)

In Section 7 of the November 10, 2003 Office Action, the Examiner rejected claims 64, 65, 76, 77, 78, 103, 104 and 105 under 35 U.S.C. 103(a) as allegedly unpatentable over Lightner, as stated above, and further in view of U.S. Patent No. 5,952,546 to Bedbrook.

The Examiner acknowledged that Lightner et al. do not teach the use of inverted repeats.

However, the Examiner alleged that Bedbrook teaches use of inverted repeats in an antisense construct to decrease expression of an endogenous gene, referring to claim 1 of Bedbrook. The Examiner then alleged that it would have been obvious to substitute the disclosure of Lightner et al. with a construct having inverted repeats, given the teachings of Bedbrook.

In response, applicants first respectfully submit that the disclosure of Lightner et al. is deficient for the reasons discussed above and fails to make applicants' new claims *prima facie* obvious, alone or in combination with Bedbrook.

Second, applicants respectfully submit that no motivation has been offered by the Examiner for combining Bedbrook with Lightner et al. The mere existence of a teaching of inverted repeats cannot make inverted repeats desirable for use in cotton plants. Actual motivation is required for a case of *prima facie* obviousness, which has not been made in this case.

Finally, even if a *prima facie* case had been made, applicants respectfully direct the Examiner's attention to applicants' disclosure, for example, on page 13, lines 9-13, and on page 113, line 31 to page 114, line 5 of the specification discussing the unexpectedly enhanced frequency of gene silencing by inverted repeats as compared to antisense. Accordingly, even if a *prima facie* case had been made, applicants' experimental data would support patentability of claims reciting use of inverted repeats.

In conclusion, the rejection under 35 U.S.C. § 103 over Lightner et al. and Bedbrook does not apply to applicants' new claims because, 1) the deficiencies of Lighter et al. fail to make a *prima facie* case of obviousness, which deficiencies are not remedied by Bedbrook, 2) no motivation is provided for combining Bedbrook with Lightner et al., and 3) even if the combination and a *prima facie* case of obviousness could be made, applicants' experimental data showing unexpected results rebuts any *prima facie* case, thus making applicants' claims reciting inverted repeats patentable.